

of the publicly accessible and searchable international sequence databases such as GenBank, the European Molecular Biology Nucleotide Sequence Database, or the DNA Database of Japan so that it can be readily accessed by the scientific community.

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Optimal Therapy for Multidrug-Resistant *Acinetobacter baumannii*

To the Editor: I read with interest the article by Doi et al. about a lung transplant patient presumed to have *Acinetobacter baumannii* ventilator-associated pneumonia (1), but some points deserve comment. *A. baumannii* is a relatively avirulent organism that frequently colonizes body fluids. For multidrug-resistant strains, antimicrobial drug selection is limited. Resolution of this patient's pulmonary infiltrates suggests that they were not caused by *A. baumannii* that persisted in respiratory secretions. Because *A. baumannii* persisted in this patient's respiratory secretions, colistin and cefepime were given. Colistin is an antimicrobial drug with low resistance potential; but when given by inhalation, it may lead to drug resistance (2,3).

Doi et al. stated that the patient's *A. baumannii* strain lacked susceptibility to all available antimicrobial drugs but that cefepime and tigecycline were intermediately susceptible (MICs 16 µg/mL and 2.0 µg/mL, respectively) (1). Intermediate susceptibility may also be interpreted as relatively susceptible when achievable serum or tissue concentrations exceed the MIC. The article did not mention the dosages of colistin, tigecycline, and cefepime. A 2-g dose of cefepime given intravenously results in peak serum levels of ≈163 µg/mL with a relatively low volume of distribution (0.29 L/kg), which would not be expected to eradicate *A. baumannii* in respiratory secretions. High-dose intravenous tigecycline (initial dose of 200 mg followed by 100 mg daily) has been used to treat *A. baumannii*, achieving peak concentrations of ≈3 µg/mL, which exceed the isolate's MIC of 2 µg/mL, and a high volume of distribution (8 L/kg), which would be expected to eradicate *A. baumannii* in respiratory secretions.

Optimal treatment for *A. baumannii* depends on susceptibility, pharmacokinetic principles, and site of infection. For optimal effectiveness, cefepime and tigecycline should have been given at high doses. To prevent potential resistance, antimicrobial drugs should not be given by inhalation (3). The alleged advantage of inhalation therapy is high local drug concentrations, but concentrations in some alveoli may be subtherapeutic (3). If possible, tigecycline should not be used to treat *A. baumannii* infections; however, if it is used, high doses should be given to optimize its pharmacokinetic attributes (4,5).

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In Response: We welcome Burke A. Cunha's letter (1) but disagree with him regarding 4 issues. First, he states that colistin has a "low resistance potential" (1). Although colistin has had low resistance for a long time, we are concerned that development of resistance to colistin is a growing problem. Heteroresistant *Acinetobacter* isolates are readily found (2). Lee et al. (3) recently found decreases in polymyxin B susceptibility during therapy.

Second, Cunha states, "Intermediate susceptibility may also be interpreted as relatively susceptible when achievable serum or tissue concentrations exceed the MIC" (1). We support the concepts that break points are artificial and that pharmacodynamic optimization may enable treatment for some organisms that are not susceptible to certain antimicrobial drugs. However, consideration of more than the MIC is necessary. Cefepime is a time-dependent bactericidal drug; therefore, effectiveness depends more on the time that the concentration of drug is above the MIC than on peak serum concentrations.

Third, Cunha states, "For optimal effectiveness, cefepime and tigecycline should have been given at high doses" (1). Unfortunately, in the current era

of antimicrobial drug resistance, there are no "shoulds." The high-dose tigecycline regimen that Cunha proposes for multidrug-resistant organisms has never, to our knowledge, been evaluated in randomized trials or even in large prospective evaluations. We all must admit that we do not know the optimal way to treat such infections and that we need rigorous evaluation of novel regimens. Anecdotal experience must not be translated into imperatives.

Fourth, Cunha states that "antimicrobial drugs should not be given by inhalation" (1). We agree that widespread use of aerosolized antimicrobial drugs cannot be recommended. However, aerosolized amikacin with a new-generation nebulizer is being tested in phase 2 clinical trials (4). As to the potential utility of aerosolized antimicrobial drugs, we prefer to keep an open mind pending the results of these trials.

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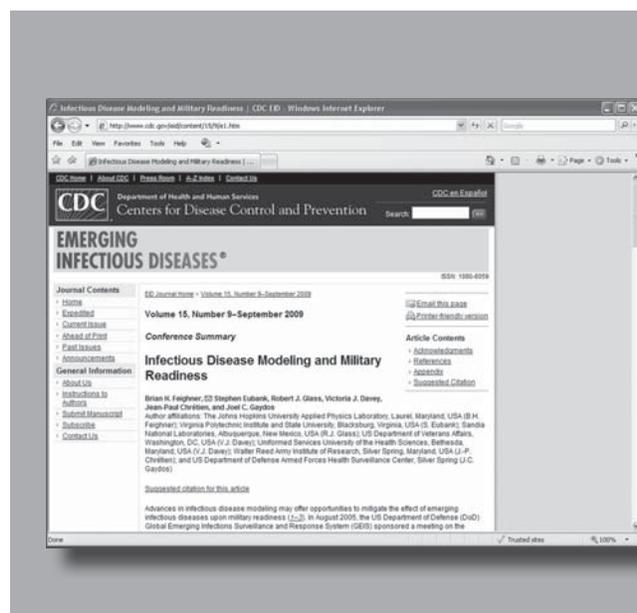
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